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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/537,697

06/06/2005

James Frances Callahan

P51395

8349

20462

7590

11/28/2007

SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER

LOEWE, SUN JAE Y

ART UNIT

PAPER NUMBER

1626

NOTIFICATION DATE

DELIVERY MODE

11/28/2007

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No. 10/537,697	Applicant(s) CALLAHAN ET AL.	
	Examiner Sun Jae Y. Loewe	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 2-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>6-6-2005; 1-25-2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-18 are pending in the instant application.

Election/Restrictions

2. Applicant's election without traverse of Group I in the reply filed on October 22, 2007 is acknowledged.
3. Claims 2-18 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter. Election was made **without** traverse in the reply filed on October 22, 2007.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on June 6, 2005 and January 25, 2007 were in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The statements were considered. Signed copies of form 1449 are enclosed herewith.

The reference of Baxter et al. was not considered because a copy was not provided.

Claim Objections

5. Claim 1 objected to because of the following informality: the claim does not end with a period. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claim 1 rejected under 35 U.S.C. 102(e) as being anticipated by Parrish et al. (WO 2003029241) - see example 1 on page 12.

The applied reference has common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

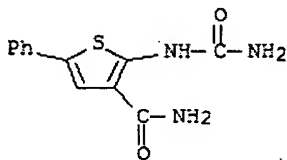
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claim 1 rejected under 35 U.S.C. 103(a) as being obvious over Parrish et al. (WO 2003029241).

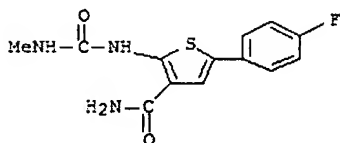
The applied reference has common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Determination of the scope and contents of the prior art.

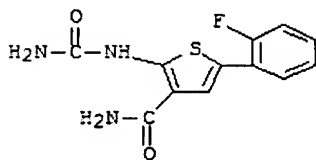
Parrish et al. teach various compounds that make obvious the instant invention. See examples below:



Second compound on p. 7



Example 1, p. 12



14th compound on p. 7

The prior art compounds are kinase inhibitors.

Ascertaining the differences between the prior art and the claims at issue.

The first compound noted above is unsubstituted at the 4-position of the phenyl ring. The instant invention has a fluorine substitution at the 4-position of the phenyl ring. Thus, relative to the prior art compound, the instant invention has a bioisosteric hydrogen-to-fluorine replacement (see Patani et al., p. 3149) at the 4-position of the phenyl ring.

The second compound noted above has a 3-methyl ureido substitution at the thiophene ring. The instant invention has a 3-ureido substitution at the thiophene ring. Thus, the instant invention is the next lower homolog of the prior art compound.

The third compound has a 2-fluorophenyl substitution at the thiophene ring. The instant invention has a 4-fluorophenyl substitution at the thiophene ring. Thus, the instant invention is a positional isomer of the prior art compound.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

It is well known in the art that bioisosteric replacements, eg. the interchange of hydrogen and fluorine, lead to compounds with equivalent biological properties (Patani et al., p. 3149). See also *Mead Johnson & Co. v. Premo Pharmaceutical Labs* (CCPS 1980) 207 USPQ 820. The prior art reference generically teaches halogen substitution. The reference further teaches several embodiments wherein the noted phenyl ring is substituted by fluorine. Thus, one of ordinary skill would be motivated to modify the prior art compound (above) to arrive at the instant invention with a reasonable expectation of success in obtaining a kinase inhibitor.

To those skilled in chemical art, one homologue is not an advance over an adjacent member of a homologous series. The reason for this is that one of ordinary skill, knowing the properties of one member of series, would know what properties to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963).

Position isomers are generally of sufficiently close structural similarity that there is a presumed expectation that such compound possess similar properties. MPEP §2144.09, *Ex parte Henkel* 130 USPQ 474, (1-phenyl-3-methyl-4-hydroxypyrazole obvious over reference teaching 3-phenyl-5-methyl-4-hydroxypyrazole). *Ex parte Weston*, 121 USPQ 429.

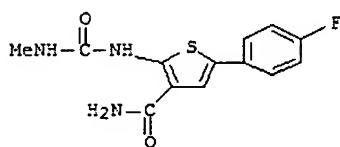
One of ordinary skill would be motivated to make the modifications above required to arrive at the instant invention with reasonable expectation of obtaining a compound that is a kinase inhibitor. The motivation would be to make additional compounds for the quoted purpose.

Thus, the instant claims are *prima facie* obvious over the teachings of the prior art.

8. Claim 1 rejected under 35 U.S.C. 103(a) as being obvious over Callahan et al. (WO 2002030353).

Determination of the scope and contents of the prior art.

Callahan et al. teach the following kinase inhibitor



2nd compound on page 8

Ascertaining the differences between the prior art and the claims at issue.

The compound noted above has a 3-methyl ureido substitution at the thiophene ring. The instant invention has a 3-ureido substitution at the thiophene ring. Thus, the instant invention is the next lower homolog of the prior art compound.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

To those skilled in chemical art, one homologue is not an advance over an adjacent member of a homologous series. The reason for this is that one of ordinary skill, knowing the properties of one member of series, would know what properties to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963).

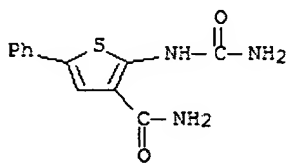
One of ordinary skill would be motivated to make the modifications above required to arrive at the instant invention with reasonable expectation of obtaining a compound that is a kinase inhibitor. The motivation would be to make additional compounds for the quoted purpose.

Thus, the instant claims are *prima facie* obvious over the teachings of the prior art.

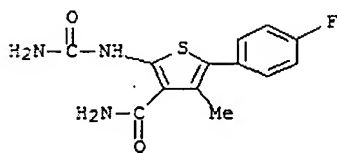
9. Claim 1 rejected under 35 U.S.C. 103(a) as being obvious over Baxter et al. (WO 2001058890).

Determination of the scope and contents of the prior art.

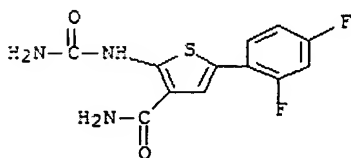
Baxter et al. teach various compounds that make obvious the instant invention. See examples below:



5th compound on p. 9



10th compound on p. 10



last compound on p. 11

The prior art compounds have the same utility as the instantly claimed invention (ie. NF-kB inhibitors).

Ascertaining the differences between the prior art and the claims at issue.

The first compound noted above is unsubstituted at the 4-position of the phenyl ring. The instant invention has a fluorine substitution at the 4-position of the phenyl ring. The third compound has a 2,4-difluorophenyl substitution at the thiophene ring. The instant invention has a 4-fluorophenyl substitution at the thiophene ring. Thus, relative to the prior art compounds, the instant invention has a bioisosteric hydrogen-to-fluorine or

fluorine-to-hydrogen replacement (see Patani et al., p. 3149) at the 4-position of the phenyl ring.

The second compound noted above has a methyl substitution at the 4 position of the thiophene ring. The instant invention is unsubstituted at the 4 position of the thiophene ring. Thus, the instant invention is the next lower homolog of the prior art compound.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

It is well known in the art that bioisosteric replacements, eg. the interchange of hydrogen and fluorine, lead to compounds with equivalent biological properties (Patani et al., p. 3149). See also *Mead Johnson & Co. v. Premo Pharmaceutical Labs* (CCPS 1980) 207 USPQ 820. The prior art reference generically teaches halogen substitution. The reference further teaches embodiments wherein the noted phenyl ring is unsubstituted, substituted once by fluorine, substituted twice by fluorine. Thus, one of ordinary skill would be motivated to modify the prior art compounds (above) to arrive at the instant invention with a reasonable expectation of success in obtaining a NF-kB inhibitor.

To those skilled in chemical art, one homologue is not an advance over an adjacent member of a homologous series. The reason for this is that one of ordinary skill, knowing the properties of one member of series, would know what properties to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963).

One of ordinary skill would be motivated to make the modifications above required to arrive at the instant invention with reasonable expectation of obtaining a compound that is a kinase inhibitor. The motivation would be to make additional compounds for the quoted purpose.

Thus, the instant claims are *prima facie* obvious over the teachings of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

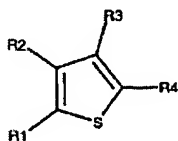
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claim 1 rejected under obviousness-type double patenting as being unpatentable over claims 2, 3, 21, 23 and 24 of copending Application No. 11/237,232. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons below.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Determination of the scope and contents of claims 2, 3, 21, 23 and 24 of US Appl. 11/237,232.
The claims are drawn to compounds of formula



(I)

Preferred embodiments claimed are the compounds shown above in section 8. The compounds are NF-kB inhibitors.

Ascertaining the differences between claims 2, 3, 21, 23 and 24 of US Appl. 11/237,232 and the claims at issue.

Preferred embodiments claimed are compounds that make obvious the instant invention (see above section 8).

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

MPEP § 2144.08.II.A.4(c) states "...consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties". This is a "Genus-Species Guidelines" for the examination based on 35 U.S.C. 103. An analogous guideline was followed here for the analysis of obviousness-type double patenting.

The preferred embodiments of US Appl. 11/237,232 suggest to one of ordinary skill to make the instantly claimed compound. Thus, the instant claims are *prima facie* obvious over claims 2, 3, 21, 23 and 24 of US Appl. 11/237,232.

Conclusion

11. No claims allowed.

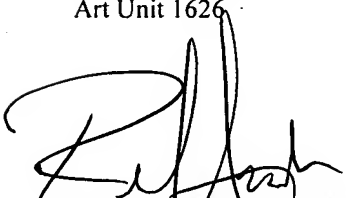
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sun Jae Y. Loewe whose telephone number is (571) 272-9074.

The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sun Jae Y. Loewe
Art Unit 1626



REBECCA ANDERSON
PRIMARY EXAMINER